

General

Guideline Title

Evaluation of individuals with pulmonary nodules: when is it lung cancer? Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines.

Bibliographic Source(s)

Gould MK, Donington J, Lynch WR, Mazzone PJ, Midthun DE, Naidich DP, Wiener RS. Evaluation of individuals with pulmonary nodules: when is it lung cancer? Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013 May;143(5 Suppl):e93S-120S. [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Gould MK, Fletcher J, Iannettoni MD, Lynch WR, Midthun DE, Naidich DP, Ost DE, American College of Chest Physicians. Evaluation of patients with pulmonary nodules: when is it lung cancer?: ACCP evidence-based clinical practice guidelines (2nd edition). Chest. 2007 Sep;132(3 Suppl):108S-30S.

Recommendations

Major Recommendations

The grades of recommendation (1A–2C) and the approach to rating the quality of evidence are defined at the end of the "Major Recommendations" field.

Anatomic Imaging

In the individual with an indeterminate nodule that is visible on chest radiography and/or chest computed tomography (CT), the panel recommends that prior imaging tests should be reviewed (Grade 1C).

In the individual with a solid, indeterminate nodule that has been stable for at least 2 years, the panel suggests that no additional diagnostic evaluation need be performed (Grade 2C).

Remark: This recommendation applies only to solid nodules. For guidance about follow-up of subsolid nodules, see recommendations listed below.

In the individual with an indeterminate nodule that is identified by chest radiography, the panel recommends that CT of the chest should be performed (preferably with thin sections through the nodule) to help characterize the nodule (Grade 1C).

Solid Nodules Measuring >8 mm in Diameter

Clinical Probability of Cancer

In the individual with a solid, indeterminate nodule that measures >8 mm in diameter, the panel suggests that clinicians estimate the pretest probability of malignancy either qualitatively by using their clinical judgment and/or quantitatively by using a validated model (Grade 2C).

Functional Imaging

In the individual with a solid, indeterminate nodule that measures >8 mm in diameter and low to moderate pretest probability of malignancy (5%–65%), the panel suggests that functional imaging, preferably with positron emission tomography (PET), should be performed to characterize the nodule (Grade 2C).

In the individual with a solid, indeterminate nodule that measures >8 mm in diameter and a high pretest probability of malignancy (>65%), the panel suggests that functional imaging should not be performed to characterize the nodule (Grade 2C).

Remark: PET may be indicated for pretreatment staging among those patients with nodules in whom malignancy is strongly suspected or confirmed.

Shared Decision-making and Patient Preferences

In the individual with a solid, indeterminate nodule that measures >8 mm in diameter, the panel recommends that clinicians discuss the risks and benefits of alternative management strategies and elicit patient preferences for management (Grade 1C).

CT Scan Surveillance

In the individual with a solid, indeterminate nodule that measures >8 mm in diameter, the panel suggests surveillance with serial CT scans in the following circumstances (Grade 2C):

- When the clinical probability of malignancy is very low (<5%)
- When clinical probability is low (<30%–40%) and the results of a functional imaging test are negative (i.e., the lesion is not hypermetabolic by PET or does not enhance >15 HUs on dynamic contrast CT), resulting in a very-low posttest probability of malignancy
- When needle biopsy is nondiagnostic and the lesion is not hypermetabolic by PET
- When a fully informed patient prefers this nonaggressive management approach

Remark: CT surveillance of solid nodules >8 mm should use low-dose, noncontrast techniques with thin sections through the nodule of interest.

In the individual with a solid, indeterminate nodule that measures >8 mm in diameter who undergoes surveillance, the panel suggests that serial CT scans should be performed at 3–6, 9–12, and 18–24 months, using thin sections and noncontrast, low-dose techniques (Grade 2C).

Remark: Serial CT scans should be compared with all available prior studies, especially the initial (index) CT scan.

Remark: Where available, manual and/or computer-assisted measurements of area, volume, and/or mass may facilitate early detection of growth.

In the individual with a solid, indeterminate nodule that shows clear evidence of malignant growth on serial imaging, the panel recommends nonsurgical biopsy and/or surgical resection unless specifically contraindicated (Grade 1C).

Remark: Solid nodules that decrease in size but do not disappear completely should be followed to resolution or lack of growth over 2 years.

Nonsurgical Biopsy

Bronchoscopy

In the individual with a solid, indeterminate nodule that measures >8 mm in diameter, the panel suggests nonsurgical biopsy in the following circumstances (Grade 2C):

- When clinical pretest probability and findings on imaging tests are discordant
- When the probability of malignancy is low to moderate (~10%–60%)
- When a benign diagnosis requiring specific medical treatment is suspected
- When a fully informed patient desires proof of a malignant diagnosis prior to surgery, especially when the risk of surgical complications is high

Remark: The type of biopsy should be selected based on nodule size, location, and relation to a patent airway; the risk of complications in the individual patient; and available expertise.

Surgical Diagnosis

In the individual with a solid, indeterminate nodule that measures >8 mm in diameter, the panel suggests surgical diagnosis in the following circumstances (Grade 2C):

- When the clinical probability of malignancy is high ($>65\%$)
- When the nodule is intensely hypermetabolic by PET or markedly positive by another functional imaging test
- When nonsurgical biopsy is suspicious for malignancy
- When a fully informed patient prefers undergoing a definitive diagnostic procedure.

In the individual with a solid, indeterminate nodule measuring ≥ 8 mm in diameter who chooses surgical diagnosis, the panel recommends thoracoscopy to obtain a diagnostic wedge resection (Grade 1C).

Remark: Use of advanced localization techniques or open thoracotomy may be necessary when resecting small or deep nodules.

Solid Nodules Measuring ≤ 8 mm in Diameter

Management Strategies

In the individual with a solid nodule that measures ≤ 8 mm in diameter and no risk factors for lung cancer, the panel suggests that the frequency and duration of CT surveillance be chosen according to the size of the nodule (Grade 2C):

- Nodules measuring ≤ 4 mm in diameter need not be followed, but the patient should be informed about the potential benefits and harms of this approach
- Nodules measuring >4 mm to 6 mm should be reevaluated at 12 months without the need for additional follow-up if unchanged
- Nodules measuring >6 mm to 8 mm should be followed sometime between 6 and 12 months and then again at between 18 and 24 months if unchanged

Remark: For the individual with multiple small, solid nodules, the frequency and duration of follow-up should be based on the size of the largest nodule.

Remark: CT surveillance of solid nodules ≤ 8 mm should use low-dose, noncontrast techniques.

In the individual with a solid nodule that measures ≤ 8 mm in diameter who has one or more risk factors for lung cancer, the panel suggests that the frequency and duration of CT surveillance be chosen according to the size of the nodule (Grade 2C):

- Nodules measuring ≤ 4 mm in diameter should be reevaluated at 12 months without the need for additional follow-up if unchanged
- Nodules measuring >4 mm to 6 mm should be followed sometime between 6 and 12 months and then again between 18 and 24 months if unchanged.
- Nodules measuring >6 mm to 8 mm should be followed initially sometime between 3 and 6 months, then subsequently between 9 and 12 months, and again at 24 months if unchanged.

Remark: For the individual with multiple small, solid nodules, the frequency and duration of follow-up should be based on the size of the largest nodule.

Remark: CT surveillance of solid nodules ≤ 8 mm should use low-dose, noncontrast techniques.

Subsolid Nodules

Recommendations for Management

In the individual with a nonsolid (pure ground glass) nodule measuring ≤ 5 mm in diameter, the panel suggest no further evaluation (Grade 2C).

In the individual with a nonsolid (pure ground glass) nodule measuring >5 mm in diameter, the panel suggest annual surveillance with chest CT for at least 3 years (Grade 2C).

Remark: CT surveillance of nonsolid nodules should use noncontrast techniques with thin sections through the nodule of interest.

Remark: Nonsolid nodules that grow or develop a solid component are often malignant, prompting further evaluation and/or consideration of resection.

Remark: Early follow-up at 3 months may be indicated for nonsolid nodules measuring >10 mm (followed by nonsurgical biopsy and/or surgical

resection for nodules that persist).

Remark: Limited duration or no follow-up may be preferred by individuals with life-limiting comorbidities in whom a low-grade malignancy would be of little consequence or by others who place a high value on avoiding treatment of possibly indolent lung cancer.

In the individual with a part-solid nodule measuring ≤ 8 mm in diameter, the panel suggests CT surveillance at approximately 3, 12, and 24 months, followed by annual CT surveillance for an additional 1 to 3 years (Grade 2C).

Remark: CT surveillance of part-solid nodules should use noncontrast techniques with thin sections through the nodule of interest.

Remark: Part-solid nodules that grow or develop a solid component are often malignant, prompting further evaluation and/or consideration of resection.

Remark: Limited duration or no follow-up may be preferred by individuals with life-limiting comorbidities in whom a low-grade malignancy would be of little consequence or by others who place a high value on avoiding treatment of possibly indolent lung cancer.

In the individual with a part-solid nodule measuring > 8 mm in diameter, the panel suggests repeat chest CT at 3 months, followed by further evaluation with PET, nonsurgical biopsy, and/or surgical resection for nodules that persist (Grade 2C).

Remark: PET should not be used to characterize part-solid lesions in which the solid component measures ≤ 8 mm.

Remark: Nonsurgical biopsy can be used to establish the diagnosis and/or be combined with wire, radioactive seed, or dye localization to facilitate subsequent resection. A nondiagnostic biopsy result does not exclude the possibility of malignancy.

Remark: Part-solid nodules measuring > 15 mm in diameter should proceed directly to further evaluation with PET, nonsurgical biopsy, and/or surgical resection.

Individuals with One or More Additional Nodules Detected During Nodule Evaluation

In the individual with a dominant nodule and one or more additional small nodules, the panel suggests that each nodule be evaluated individually and curative treatment not be denied unless there is histopathological confirmation of metastasis (Grade 2C).

Remark: The classification and appropriate treatment of patients with more than one pulmonary focus of lung cancer is difficult and requires multidisciplinary consideration.

Definitions:

Strength of the Recommendations Grading System

Grade of Recommendation	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Strong recommendation, high-quality evidence, Grade 1A	Benefits clearly outweigh risk and burdens or vice versa	Consistent evidence from randomized controlled trials (RCTs) without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Benefits clearly outweigh risk and burdens or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Recommendation can apply to most patients in most circumstances. Higher quality research may well have an important impact on confidence in the estimate of effect and may change the estimate
Strong recommendation, low- or very-low-quality evidence, Grade 1C	Benefits clearly outweigh risk and burdens or vice versa	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate
Weak recommendation, high-quality evidence, Grade 2A	Benefits closely balanced with risks and burden	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient's or societal values. Further research is very unlikely to change confidence in the estimate of effect

Weak Recommendation	Grade of Recommendation	Benefits, Risk and Burden	Evidence Limitations	Methodologic Quality of Supporting Evidence	Best action may differ on circumstances or patient's or societal values.	Implications
moderate-quality evidence, Grade 2B		burden		methodologic flaws, indirect or imprecise) or very strong evidence from observational studies		Higher-quality research may well have an important impact on confidence in the estimate of effect and may change the estimate
Weak recommendation, low- or very-low-quality evidence, Grade 2C		Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced		Evidence for at least one critical outcome from observational studies, case series, or RCTs, with serious flaws or indirect evidence		Other alternatives may be equally reasonable. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate

Clinical Algorithm(s)

The following clinical algorithms are provided in the original guideline document:

- Management algorithm for individuals with solid nodules measuring 8 mm to 30 mm in diameter
- Management algorithm for individuals with solid nodules measuring <8 mm in diameter

Scope

Disease/Condition(s)

Pulmonary nodules

Guideline Category

Diagnosis

Evaluation

Management

Clinical Specialty

Family Practice

Oncology

Pathology

Pulmonary Medicine

Radiology

Thoracic Surgery

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Nurses

Patients

Physicians

Guideline Objective(s)

- To inform the clinical decisions that must be jointly made by physicians and patients in developing diagnostic, treatment, and management plans so that they can enhance the benefits and reduce the harms associated with various options
- To update previous evidence-based recommendations for evaluation and management of individuals with solid pulmonary nodules and to generate new recommendations for those with nonsolid nodules

Target Population

Individuals with pulmonary nodules

Interventions and Practices Considered

1. Review of prior imaging results
2. Chest x-ray (CXR)
3. Chest computed tomography (CT)
4. Estimation of pretest probability of malignancy
5. Functional imaging, preferably positron emission tomography (PET)
6. Discussion of risks and benefits of management strategies with patient
7. CT surveillance
8. Nonsurgical biopsy and/or surgical resection
9. Thoracoscopy

Major Outcomes Considered

Sensitivity and specificity of diagnostic tests
Diagnostic yield

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

A multidisciplinary writing committee comprising four pulmonologists, two thoracic surgeons, and one radiologist formulated questions (see Table S1 in the supporting data [see the "Availability of Companion Documents" field]).

To update previously published guidelines for evaluation of individuals with pulmonary nodules, the panel repeated prior searches of MEDLINE for studies of chest computed tomography (CT) imaging, positron emission tomography (PET) imaging, and transthoracic needle biopsy (TTNB) and performed new searches for studies of subsolid nodules, bronchoscopy, surgical complications, and methods to detect nodule growth (see Appendix S1 in the supporting data [see the "Availability of Companion Documents" field]). All searches were performed in October 2011 and

subsequently updated through May 2012. The panel identified additional articles by searching their own personal files and by reviewing reference lists of included studies. The panel included all randomized controlled trials, controlled observational studies, uncontrolled studies of diagnostic accuracy, and cross-sectional studies that examined relationships between nodule morphology and outcomes.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Not Given)

Rating Scheme for the Strength of the Evidence

Not stated

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

A multidisciplinary writing committee comprising four pulmonologists, two thoracic surgeons, and one radiologist synthesized and reviewed available evidence.

Assessment of Study Quality

Systematic reviews and meta-analyses were assessed using Documentation and Appraisal Review Tool (DART)(R. L. Diekemper; B. K. Ireland, MD; and L. R. Merz, PhD, MPH, DART, unpublished data, 2012), which was developed as an improved alternative to the existing tools for use in a clinical setting. However, this tool has been adopted for use in American College of Chest Physicians (ACCP) guidelines and consensus statements since 2011.

Quality was assessed for each study as well as for the body of relevant evidence. Based on the population, intervention, comparator, and outcome (PICO) questions and volume of available literature, multiple study designs were included in the systematic reviews of the literature. Randomized controlled trials (RCTs) primarily indicate benefits, but whenever observational studies met inclusion criteria they were often helpful in identifying harms. Observational studies were also examined when RCTs were not available to answer a particular PICO question. Allowing for multiple study designs resulted in the need for multiple quality assessment tools. Tools were chosen for assessing RCTs, observational studies, and diagnostic studies. The quality assessment tool for RCTs (R. L. Diekemper, B. K. Ireland, and L. R. Merz, unpublished data, 2012) was used for assessing the quality of RCTs, and a tool developed by the committee of the ninth edition of the Antithrombotics Guidelines was used for assessing the quality of observational studies. Diagnostic studies were assessed using the Quality Assessment Tool for Diagnostic Accuracy Studies (QUADAS).

Meta-analyses

If a recently published good-quality meta-analysis was available, then it was used to inform the recommendations. When a good-quality meta-analysis was not available, guideline authors were encouraged to perform their own meta-analyses. Meta-analyses were performed when the data were fairly homogeneous. If a study was deemed poor quality, then it was not included in the pooled analysis. Heterogeneity of the pooled results was assessed using a χ^2 test and Higgins I^2 , and a forest plot was examined for consistency of the results. The random effects model was chosen a priori as the appropriate model for pooling the data because it accounts for heterogeneity among the included studies. Results from the meta-analyses are available in the supplementary materials that can be downloaded from the Journal website under the corresponding article in the table of contents.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

A multidisciplinary writing committee comprising four pulmonologists, two thoracic surgeons, and one radiologist developed or revised recommendations, rated the quality of evidence, and graded the strength of the recommendations by using a standardized approach. The writing committee reviewed all recommendations and reached consensus by iterative discussion and debate. The manuscript was extensively revised, although some sections of text (including much of the section on solid nodules measuring ≤ 8 mm in diameter) were considered to be current and, therefore, retained from the previous version.

Panel Composition and Responsibilities

A call for applications to serve on the 3rd edition of the American College of Chest Physicians (ACCP) Lung Cancer Guidelines (LC III) panel was put forth to the ACCP membership, to past panelists, and to other organizations that have previously endorsed earlier editions of these guidelines or appointed representatives to serve on those panels. Guiding the team was the LC III Executive Committee, composed of a Panel Chair, Vice Chair, Liaison to the Guidelines Oversight Committee (GOC), and two staff members, one serving as an adviser and the other as the lead methodologist. The GOC appointed the Liaison and the Chair, who was required to be free of conflicts of interest (COI). This Executive Committee provided general oversight and guidance; multiple reviews of research questions, article outlines, manuscripts, evidence tables, and other supporting documents; and facilitation of the final conference discussions and voting. As the scope was defined, content experts in each major area were identified to serve as topic editors and nominated by the Panel Chair to be advanced to the GOC for the requisite qualifications and COI review and approval process. These topic editors organized their research and writing teams, oversaw the work of the individual members, edited separate contributions into synthesized manuscripts, presented evidence at the final conference, and managed any of their committee members who were approved with management stipulations relevant to their COIs.

Each topic editor was initially charged with proposing individuals to support their topic committees with expertise in the content area and/or methodology. With the Chair's approval, these individuals were nominated for GOC reviews for COI and expertise. In some cases, GOC staff helped to locate additional methodologic support when it was determined to be necessary for various article committees. This resulted in an international panel of >100 multidisciplinary experts across 24 articles representing the fields of pulmonary medicine, critical care medicine, thoracic surgery, medical and radiation oncology, pathology, integrative medicine, primary care, health-care research, guidelines methodology, and epidemiology. Nineteen international organizations that are also dedicated to advancing research and practice in the area of lung cancer were invited to appoint representatives to this guideline project as adjunct participants. These individuals, unless already approved panelists, were not considered full voting members of the panel, since they had not been through the same ACCP COI review, but were included at the final conference, participated fully in the discussions, and provided external review and feedback on the manuscripts and supporting documentation.

Formulating the Recommendations

In most cases the topic editors, along with the other completely non-conflicted members of the article committee, formulated the recommendations. The summarized evidence tables and profiles (where profiles existed) provided the foundation for the recommendations. In formulating the recommendations, panelists considered not only the body of evidence but also the balance between the benefits and harms and considerations of other factors, such as cost or resource availability considerations and patient values and preferences, which might vary widely for some recommendations. These additional considerations are described in a Remarks section, which appears just below the relevant recommendation in the publication, each time the recommendation appears.

Grading the Recommendations

Recommendations that are strong must be differentiated from those that are weak or weaker. Thus, the ACCP Grading System was used (see the "Rating Scheme for the Strength of the Recommendations" field), and the wording of the recommendations is explicit. This grading system has been used since 2005 and is based on two dimensions: the balance of benefits to harms and the quality of the evidence base. If the benefits clearly outweigh the harms or the harms clearly outweigh the benefits, the strength of the recommendation is considered strong and graded as a 1. In most cases, when there is strong confidence that the benefits outweigh the harms, most patients would choose the intervention endorsed in that recommendation. However, when the tradeoffs between desirable and undesirable consequences are not as clear, variability in patient preferences and values often becomes germane to the decision-making conversation.

Weak recommendations are those for which the benefits and harms are more equally balanced, and thus a clear choice is not as obvious; these are graded with a 2. Strong recommendations are phrased, "the panel recommends," whereas weak recommendations are phrased "the panel

suggests." Accompanying these indications of the strength of a recommendation is a letter score (A, B, or C) representing the grading of the body of relevant literature.

In grading the quality of the evidence, RCTs start with a high score but might be downgraded to moderate or even low based on the following criteria: limitations in the study design or conduct of the trial, imprecision, indirectness relative to the specifics of the PICO question, inconsistency in the results, and risk of reporting bias. Observational studies, on the other hand, start off as low-level evidence but can be upgraded to moderate or even high if exceptionally large and consistent treatment effects increase confidence in the findings, especially if there is a strong dose-response gradient.

The final grades are combinations reflecting the strength of the recommendation and the quality of the evidence. Strong recommendations with high quality evidence, grade of 1A, are less common than in past editions of these guidelines, since the evidence is assessed with greater rigor for most topics, and few studies without important limitations are available.

However, recommendations that do attain this score are those for which the panel could state with confidence that new studies would be unlikely to change the direction of the effect. These recommendations apply to most patients in most circumstances. But as the grades decline, patient values and preferences likely would play an increasingly greater role in determining the best treatments or interventions for each patient.

The Final Conference

As the evidence reviews were completed and the tables and profiles prepared, the manuscripts and recommendations were drafted. Members of the article committees convened by phone or e-mail to discuss the evidence and work on drafting and grading the recommendations. These discussions generally resulted in agreement on both the quality of the evidence and strength of the recommendations.

The manuscripts and supporting tables were then reviewed by members of the Executive Committee and, after several iterations, the revised versions were shared among all panelists and the representatives of invited organizations in advance of the conference. The other panelists and representatives were asked not only to provide feedback but also to review the recommendations to identify any controversies. A recommendation was deemed to be controversial if at least one person disagreed with the wording or the grading, if there was controversy in practice, if there were wide variations in practice, or if at least one person asked that it be discussed among the broader panel and association representatives. These identified controversies composed the main agenda for the conference.

See the "Methodology for Development of Guidelines for Lung Cancer" (see the "Availability of Companion Document" field) for more information.

Rating Scheme for the Strength of the Recommendations

Strength of the Recommendations Grading System

Grade of Recommendation	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Strong recommendation, high-quality evidence, Grade 1A	Benefits clearly outweigh risk and burdens or vice versa	Consistent evidence from randomized controlled trials (RCTs) without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Benefits clearly outweigh risk and burdens or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Recommendation can apply to most patients in most circumstances. Higher quality research may well have an important impact on confidence in the estimate of effect and may change the estimate
Strong recommendation, low- or very-low-quality evidence, Grade 1C	Benefits clearly outweigh risk and burdens or vice versa	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate
Weak recommendation, high-quality	Benefits closely balanced with risks and burden	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from	The best action may differ depending on circumstances or patient's or societal values. Further research is very unlikely to change

evidence, Grade 2A Grade of Recommendation	Benefit vs. Risk and Burdens	observational studies Methodologic Quality of Supporting Evidence	confidence in the estimate of effect Implications
Weak recommendation, moderate-quality evidence, Grade 2B	Benefits closely balanced with risks and burden	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence from observational studies	Best action may differ depending on circumstances or patient's or societal values. Higher-quality research may well have an important impact on confidence in the estimate of effect and may change the estimate
Weak recommendation, low- or very-low-quality evidence, Grade 2C	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Evidence for at least one critical outcome from observational studies, case series, or RCTs, with serious flaws or indirect evidence	Other alternatives may be equally reasonable. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate

Cost Analysis

Use of fluorodeoxyglucose-positron emission tomography (FDG-PET) scanning may be most cost-effective when clinical pretest probability and computed tomography (CT) scan results are discordant, especially when pretest probability is relatively low and CT image characteristics are indeterminate (i.e., not clearly benign).

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Internal and External Peer Review

Once Executive Committee approval was received, the articles were submitted to American College of Chest Physicians (ACCP) staff for several layers of review. All reviewers were required to undergo a full conflict of interest (COI) appraisal before being approved. In the first round of reviews, the Thoracic Oncology NetWork reviewed the content of the manuscripts and the members of the Guidelines Oversight Committee (GOC) assessed the manuscripts for adherence to the methodology and conformance with the evidence. The ACCP President also appointed members of the Board of Regents to evaluate the guidelines in depth. All comments were collated into spreadsheets to ensure that they were appropriately answered. GOC and board reviewers discussed each comment and determined which should be mandatory for the authors to amend and which were provided as suggestions for improvement. All reviews and comments were anonymous, and authors were required to respond to all mandatory issues either by revising the manuscripts or providing written justification explaining why they did not agree with the reviewers' comments.

The revised manuscripts were submitted for round II review, simultaneously with the Journal peer review. Once the GOC and board reviewers approved the manuscripts, the ACCP President, President Elect, President Elect Designee, and Immediate Past President reviewed the guidelines. Approval was granted pending confirmation from the Board of Regents, before submission to the journal for final review by the Journal Editor. In addition to this extensive review process, which included nearly 30 individual reviewers from the ACCP leadership, external organizations were provided with opportunities to provide feedback before, during, and just after the conference. This final version was submitted for consideration for endorsement to all of the invited organizations, whether or not they sent representatives to the conference. However, once the guidelines were approved by the ACCP Board of Regents, no further changes were accepted. Organizations that provided endorsements are listed in each article.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate evaluation of individuals with pulmonary nodules

Potential Harms

- Risks associated with computed tomography (CT) scan include radiation exposure and adverse effects because of administration of iodinated contrast material. The risk of radiation-induced cancer is uncertain in magnitude.
- Across 24 studies that reported adverse events of bronchoscopy with biopsy guided by radial endobronchial ultrasound (EBUS), electromagnetic navigation bronchoscopy (ENB), guide sheath, ultrathin bronchoscopy, or virtual bronchoscopy navigation (VBN), the pooled risk of pneumothorax was 1.6%, and the risk of pneumothorax requiring chest tube placement was 0.7%.
- False-negative or false-positive results of imaging and measurement methods
- Complications of transthoracic needle biopsy (TTNB) include pneumothorax and hemorrhage.
- Risk of surgical complications

Contraindications

Contraindications

Intravenous contrast is relatively or absolutely contraindicated in patients with renal insufficiency or allergy to iodine, and it is usually not necessary to administer contrast when performing follow-up computed tomography (CT) scans to identify growth.

Qualifying Statements

Qualifying Statements

- American College of Chest Physicians (ACCP) guidelines are intended for general information only, are not medical advice, and do not replace professional medical care and physician advice, which always should be sought for any medical condition. The complete disclaimer for this guideline can be accessed at the [CHEST Web site](#) .
- Although the ACCP is moving toward the production of evidence profiles for all guideline recommendations, there were many recommendations for which profiles were not developed, mostly because of resource constraints. When possible, methodologists created evidence profiles, and all panelists were educated on how to read and interpret them. The population, intervention, comparator, and outcome (PICO)-based systematic literature review process was followed for most recommendations, but there were some that could have benefited from meta-analyses.
- One limitation of all guidelines today is that they are not able to adequately address complex patients with multiple morbidities. This is largely because these patients are generally excluded from clinical trials and are often not included in observational studies. Since guidelines are reliant on evidence published in the peer-reviewed literature, the scientific foundation impedes the process of providing good guidance for these patients and is a limitation in these guidelines. Therefore, the ACCP encourages funding agencies to ensure that topics with limited evidence are addressed in future research.

Implementation of the Guideline

Description of Implementation Strategy

Dissemination and Implementation

These guidelines are widely disseminated through the *CHEST* journal publication, National Guideline Clearinghouse, and Guidelines International Network library. Additional clinical resources will soon be available to users of CHEST Evidence, an upcoming tool for searching the content of American College of Chest Physicians (ACCP) guidelines.

As the expanding research into diagnostic techniques and treatment options continues to evolve, the guidelines must be updated and kept current. This edition of the ACCP Lung Cancer Guidelines will be the last to be published as a complete collection, as the ACCP is now embarking on a new living guidelines model (LGM) for revising existing recommendations and developing new recommendations as the literature evolves. This will include a continual assessment of the currency of these recommendations relevant to new research studies as they are published. The review cycle for the ACCP Lung Cancer Guidelines will begin 1 year after publication unless the content experts who monitor the literature bring a recommendation or set of related recommendations to the attention of the Guideline oversight Committee (GOC), suggesting that those recommendations are in need of updating sooner. The new LGM will permit a more nimble approach to guideline development but also requires a point-of-care accessible vehicle, CHEST Evidence, for the users to readily search for the most current version. These features will be described in greater detail in upcoming publications. As a step in this direction, these guidelines will be published primarily online with a printed version of the Executive Summary, containing all of the recommendations, the introduction, and this article on methodology. All narratives for each article with their supporting tables, figures, and algorithms will be available online at journal.publications.chestnet.org .

Implementation Tools

Clinical Algorithm

Mobile Device Resources

Patient Resources

Quick Reference Guides/Physician Guides

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Patient-centeredness

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

Gould MK, Donington J, Lynch WR, Mazzone PJ, Midthun DE, Naidich DP, Wiener RS. Evaluation of individuals with pulmonary nodules: when is it lung cancer? Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2003 Jan (revised 2013 May)

Guideline Developer(s)

American College of Chest Physicians - Medical Specialty Society

Source(s) of Funding

- The development of this guideline was supported primarily by the American College of Chest Physicians (ACCP). The lung cancer guidelines conference was supported in part by a grant from the Lung Cancer Research Foundation. The publication and dissemination of the guidelines was supported in part by a 2009 independent educational grant from Boehringer Ingelheim Pharmaceuticals, Inc.
- Role of sponsors: The ACCP was solely responsible for the development of these guidelines. The remaining supporters played no role in the development process. External supporting organizations cannot recommend panelists or topics, nor are they allowed prepublication access to the manuscripts and recommendations. Further details on the Conflict of Interest (COI) Policy are available online at <http://chestnet.org> .
- See the methodology companion (see the "Availability of Companion Documents" field) for a complete discussion of the source of funding for this guideline.

Guideline Committee

American College of Chest Physicians (ACCP) Expert Panel on Lung Cancer Guidelines

Composition of Group That Authored the Guideline

Authors: Michael K. Gould, MD, FCCP; Jessica Donington, MD; William R. Lynch, MD; Peter J. Mazzone, MD, MPH, FCCP; David E. Midthun, MD, FCCP; David P. Naidich, MD, FCCP; Renda Soylemez Wiener, MD, MPH

Financial Disclosures/Conflicts of Interest

- Conflicts of Interest (COI) grids reflecting the conflicts of interest that were current as of the date of the conference and voting are posted in the online supplementary materials.
- Financial/nonfinancial disclosures: The authors have reported to *CHEST* the following conflicts of interest: Dr Mazzone participated in an advisory board meeting organized by Oncimmune (USA) LLC and received research funding from Metabolomx. Dr Naidich has served as a consultant for law firms and for Siemens Medical Solutions in the development of methods for computer-assisted detection of lung nodules. Drs Gould, Donington, Lynch, Midthun, and Wiener have reported that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.
- See the methodology companion (see the "Availability of Companion Documents" field) for a complete discussion of the conflict of interest procedures and requirements for the guideline panel.

Guideline Endorser(s)

American Association for Bronchology and Interventional Pulmonology - Medical Specialty Society

European Society of Thoracic Surgeons - Professional Association

Oncology Nursing Society - Professional Association

Society of Thoracic Surgeons - Medical Specialty Society

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Gould MK, Fletcher J, Iannettoni MD, Lynch WR, Midthun DE, Naidich DP, Ost DE, American College of Chest Physicians. Evaluation of patients with pulmonary nodules: when is it lung cancer?: ACCP evidence-based clinical practice guidelines (2nd edition). Chest. 2007 Sep;132(3 Suppl):108S-30S.

Guideline Availability

Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#) . Also available to Chest subscribers through the [Chest app](#) for iPhone and iPad.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

Availability of Companion Documents

The following are available:

- Evaluation of individuals with pulmonary nodules: when is it lung cancer?: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Supporting data. Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#) .
- Detterbeck FC, Zelman Lewis S, Diekemper R, Addrizzo-Harris D, Alberts MW. Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Executive summary. Chest 2013 May;143(5 Suppl):7S-37S. Electronic copies: Available from the [Chest - The Cardiopulmonary and Critical Care Journal Web site](#) .
- Alberts WM. Introduction to the third edition: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):38S-40S. Electronic copies: Available from the [Chest - The Cardiopulmonary and Critical Care Journal Web site](#) .
- Zelman Lewis S, Diekemper R, Addrizzo-Harris DJ. Methodology for development of guidelines for lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians. Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):41S-e50S. Electronic copies: Available from the [Chest - The Cardiopulmonary and Critical Care Journal Web site](#) .
- Alberg AJ, Brock MV, Ford JG, Samet JM, Spivack SD. Epidemiology of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):e1S-e29S. Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#) .
- Nana-Sinkham SP, Powell CA. Molecular biology of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013 May;143(5 Suppl):e30S-e39S. Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#) .

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

The following is also available:

- Highlights of the ACCP diagnosis and management of lung cancer guidelines, 3rd ed. Podcast. Available from the [Chest - The Cardiopulmonary and Critical Care Journal Web site](#) .

Patient Resources

The following is available:

- Lung cancer: understanding the diagnosis. Northbrook (IL): American College of Chest Physicians; 2010. 7 p. Electronic copies: Available in Portable Document Format (PDF) from the [OneBreath.org Web site](#) .

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NGC Status

This NGC summary was completed by ECRI on June 30, 2003. The information was verified by the guideline developer on July 25, 2003. This NGC summary was updated by ECRI Institute on November 7, 2007. The updated information was verified by the guideline developer on December 21, 2007. This NGC summary was updated by ECRI Institute on August 21, 2013.

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